

## AGEING SERIES

## Ageing and the gut

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Postgrad Med J 2007;83:44–53. doi: 10.1136/pgmj.2006.049361

The current concepts on diagnosis, clinical features, and management of common gastrointestinal conditions in the elderly population, taking into account physiological aspects of ageing, are evaluated. Gastrointestinal (GI) disorders are discussed with an emphasis on oesophageal problems, *Helicobacter pylori* infection, malabsorption, diverticular disease, and cancer. GI problems are acquiring greater importance in hospitals and in the community and their incidence is increasing. Newer treatments have less impact on patients' wellbeing and meticulously planned investigation and treatment is needed. Careful selection of patients and application of modern techniques has improved survival and outcomes, with comparable results to those in younger age groups.

Ageing and the accompanying decline of various physiological processes has important effects on the gastrointestinal (GI) tract. These and the atypical manifestations of common conditions in older people have implications for diagnosis and management. The demographic trends towards an ageing population and an increasing incidence and prevalence of GI disease in the elderly are important considerations. Although the established definition of "elderly" referred to people above the age of 65, current demographic trends, improved health care, and our understanding of the distinction between biological age and chronological age dictates that this be revised to a chronological age of >75.<sup>1</sup> This review aims at highlighting the various factors responsible for GI disease in this age group and the management of common clinical problems encountered.

## METHODS

A MEDLINE (1966–2006) search was performed using search words "gastrointestinal disease", "elderly", "GERD", "peptic ulcer disease", "malabsorption", "diarrhea", "constipation", "IBS", "inflammatory bowel disease", "bowel ischemia", and "colorectal cancer". Reviews and original papers, in the English language, especially those on gastrointestinal problems commonly encountered, were identified. Foreign language papers with an English abstract were also identified. Bibliographic details from certain papers were examined and background information extracted from texts like the *Merck Manual*. A basic search was also performed on Google using the terms "gastrointestinal disease" and "ageing".

## ORAL CAVITY

Various symptoms and signs arise in the mouth either from local or systemic disease. Common problems include *soreness and ulceration, problems with salivation, mastication, swallowing, and taste*.

Soreness can result from ill fitting dentures and also vitamin deficiencies, with resultant mucosal changes. There is reduced salivary secretion either as a result of physiological changes with age or through the use of drugs with anti-cholinergic effects (for example, antidepressants), all of which contribute to difficulties with swallowing. Although elderly people complain of dry mouth, salivary secretion is actually unchanged in response to stimuli. However, basal salivary gland secretion, sense of taste and smell are all reduced with age.<sup>2</sup> Pathological processes certainly contribute; more importantly, these include neurological disease affecting the lower cranial nerves or their central connections. Consequently, the progression is towards anorexia and thereby malnutrition.

One of the more commonly encountered problems in clinical practice is *dysphagia*, which is a subjective feeling ranging from difficulty initiating a swallow (oropharyngeal dysphagia) to the sensation of food sticking in transit to the stomach (oesophageal dysphagia). A detailed history will elucidate the cause in about 80–85% of cases.<sup>3</sup> Symptom onset and progression will further differentiate causes: sudden onset of oropharyngeal dysphagia results from a stroke, whereas a more gradual onset is seen in Parkinson's or neuromuscular disease such as myasthenia, or indeed, muscular dystrophy.

Videofluoroscopic examination was considered the preferred method for assessing oropharyngeal swallowing, but recently fiberoptic endoscopic evaluation of swallowing has also gained in popularity. This is an effective means of evaluating an elderly patient with dysphagia or aspiration. The procedure involves the transnasal passage of a fiberoptic laryngoscope, to visualise the hypopharynx, larynx, and proximal trachea. It can also be extended to test laryngopharyngeal sensory function: pulses of air are blown through the aryepiglottic folds to elicit the laryngeal adductor reflex; the greater the pressure of air required, the greater the degree of sensory loss. These procedures have been evaluated in various studies and have proved to be safe. They allow assessment of swallowing

**Abbreviations:** CRC, colorectal cancer; CT, computed tomography; GI, gastrointestinal; GORD, gastro-oesophageal reflux disease; IBS, irritable bowel syndrome; LOS, lower oesophageal sphincter; NOMI, non-occlusive mesenteric ischaemia; NSAIDs, non-steroidal anti-inflammatory drugs; PPIs, proton pump inhibitors

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Received 5 May 2006  
Accepted 29 August 2006

frequency and identification of the presence and severity of pooled oropharyngeal secretions, which in itself, is predictive of aspiration.<sup>4</sup>

A recent review concluded that both videofluoroscopy and fibreoptic endoscopic evaluation of swallowing are equally important tools for the assessment of oropharyngeal dysphagia.<sup>5</sup> Management consists of treating the underlying condition; however, the clinical course can be quite protracted. Complications include the need for other artificial means of feeding with its inherent problems, voice and speech problems, malnutrition, and aspiration pneumonia with consequent increased morbidity.

## OESOPHAGUS

This serves as a conduit for solids and liquids, and the normal peristaltic movements protect the airway from stomach contents. The upper end of the oesophagus, composed of striated muscle and innervated by the ninth and tenth cranial nerves, functions as the upper oesophageal sphincter. The lower end is made up of smooth muscle with the lower oesophageal sphincter forming an anatomical and physiological valve to the stomach. The oesophageal phase of deglutition is coordinated by the swallowing centre in the medulla. It follows the oropharyngeal phase and involves peristaltic contractions that propel the food bolus down to the stomach.<sup>6</sup> Possible causes of oesophageal dysphagia include neuromuscular disorders like achalasia, diffuse oesophageal spasm, and lower oesophageal sphincter (LOS) hypertension. Intrinsic obstructive lesions include tumours, strictures, and lower oesophageal ring (Schatzki's ring), while extrinsic compression can result from an enlarged aorta or left atrium as well as mediastinal mass (tumour, lymph nodes, retrosternal thyroid).

Age related changes are important and it has been demonstrated that inadequate coordination of cricoid cartilage and pharyngeal muscles, decreased peristalsis, and uncoordinated contractions can also be contributory.<sup>7</sup> Elderly people may also report accompanying odynophagia (painful swallowing), which suggests mucosal disruption and is commonly a result of pill-induced oesophagitis in this age group.

## Gastro-oesophageal reflux disease

A considerable problem in the elderly patient is gastro-oesophageal reflux disease (GORD). The cost of the medical resources used in this condition is high because it is a chronic disease and can be associated with complications like erosive oesophagitis, strictures and, more importantly, Barrett's oesophagus.<sup>8,9</sup> At least 15% of the population world wide has heartburn, the principal symptom of GORD,<sup>10</sup> though in elderly patients regurgitation, dysphagia, vomiting, and chest pain are more common than heartburn.<sup>11</sup>

The condition is known to arise from spontaneous complete relaxations of a normal LOS, the main anti-reflux barrier, which is augmented by extrinsic compression from the diaphragm.<sup>12</sup> Physiological reflux can occur owing to transient relaxations of the LOS, but in affected patients these last longer and are known to occur more often. Symptoms commonly arise not only from exposure to gastric acid but also owing to the duration of such an occurrence. Symptoms of reflux disease are typical, exacerbated by meals and recumbency, and relieved by antacids but do not warrant any investigations in most cases.<sup>13</sup>

Disease severity and symptoms have a poor correlation in the elderly and the initial presentation is rarely predictable. Indeed, the condition may first come to light because of a complication or indeed GI haemorrhage.<sup>14</sup> Strictures occur in around 10% of patients with reflux disease and are responsive to periodic dilatations by oesophago-gastro-duodenoscopy and acid suppression using proton pump inhibitors (PPIs). Studies have shown a decrease in the frequency and severity of recurrences

of strictures in patients treated this way; in this respect, PPIs were significantly better than ranitidine ( $p < 0.0001$ ) (figs 1 and 2).<sup>15</sup>

## Barrett's oesophagus

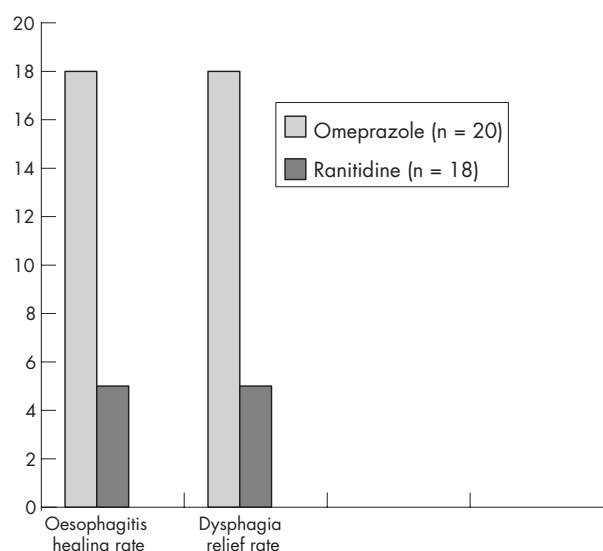
In those cases where the problem is persistent, a search for malignant transformation must be made through mucosal biopsies. Barrett's oesophagus constitutes metaplastic changes in the oesophageal mucosa that result from chronic reflux and is seen in 10–15% of patients undergoing upper GI endoscopy for GORD.<sup>16</sup> It is the most important predisposing factor for the development of adenocarcinoma of the oesophagus and the incidence of this particular malignancy is increasing.<sup>17</sup> The diagnosis and follow-up is confounded by the problem of short-segment Barrett's (intestinal metaplasia confined to a segment  $< 3$  cm); where the clinical progression of this variant to frank adenocarcinoma is uncertain.<sup>18</sup> Follow-up is important in all patients with complications, until life expectancy is not expected to exceed any benefit of further intervention. However, recent studies have shown that there is little support for screening programmes but modest benefit from continued surveillance at added cost.<sup>19</sup>

## Oesophagitis

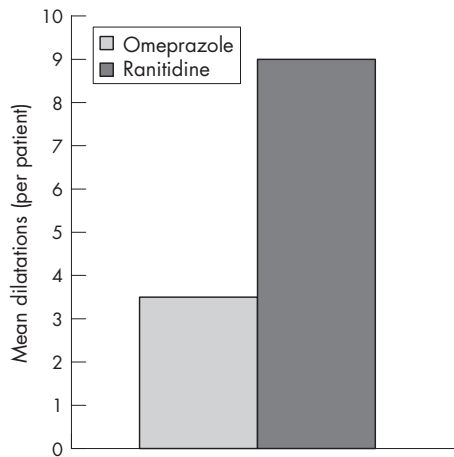
Oesophagitis, primarily the non-erosive variety, also associated with GORD, is more common in men and in one study was unrelated to age.<sup>20</sup> However, this condition is commonly seen in the older patient owing to a breakdown of various protective mechanisms combined with contributory risk factors like polypharmacy.

Diagnosis of most oesophageal disorders is with the help of oesophago-gastro-duodenoscopy, which remains the preferred method, for those patients with reflux symptoms as well as for conditions requiring confirmatory biopsy. When testing is inconclusive or for those patients considering surgery, oesophageal pH monitoring can demonstrate acid reflux.

Treatment requires a long term management plan and involves lifestyle modification, use of antacids, and PPIs. Surgical treatment is now also an option, particularly in the fit elderly patient, with comparable results to medical treatment.<sup>21</sup> Open or laparoscopic fundoplication—where the gastric fundus is wrapped around the lower oesophagus to reconstruct the gastro-oesophageal junction—is well known and offers



**Figure 1** Omeprazole v ranitidine in chronic GORD (after dilatation, 12 months' follow-up).<sup>15</sup>



**Figure 2** Mean (SD) dilatations required in the omeprazole group (3.5 (2.1)) v ranitidine group (9.0 (2.6)) after 12 months of treatment \*.<sup>15</sup>

good permanent control of reflux symptoms. Both the Toupet (270° wrap-around) and Nissen (360° wrap-around) techniques are practised. In a recent study no difference in long term outcome was found in comparison with medical treatment and the results often depended on the surgeon and had no great cost advantage.<sup>22</sup>

More recent advances include endoluminal treatments like the use of Enteryx (an inert polymer) injected around the lower oesophageal sphincter, and administration of a Stretta radio-frequency current to the mucosa at this level<sup>23</sup>; studies of their long term effect on symptoms are being undertaken. Of recent interest is whether oesophagitis occurs more frequently in those patients taking drugs such as bisphosphonates and non-steroidal anti-inflammatory drugs (NSAIDs),<sup>24</sup> and the indications are that it does. Furthermore, the effect of these drugs can be synergistic.

There are considerable geographical differences in the prevalence of oesophageal disorders like GORD and its complications, which are more common in white patients (12.3%) than in Asians (4.8%) and Afro-Caribbeans (2.8%) ( $p < 0.001$ ).<sup>25</sup> Dietary factors and a high body mass index may explain this. Furthermore, the pattern of *H. pylori* infection in Asians is predominantly one of proximal gastric inflammation causing an atrophic pan-gastritis; studies have shown this to be negatively associated with reflux oesophagitis.<sup>26</sup> Peptic ulcer disease is uncommon in African black subjects despite a high incidence of *H. pylori*; the reasons for this are unclear.<sup>27</sup>

### Malignancy

Malignancy affecting the oesophagus is more common in Japan and the Far East. In the Western world there are significant racial differences in the type of carcinoma occurring, with squamous cell tumours being more common in African-Americans and adenocarcinoma in white subjects.<sup>28</sup>

Predisposing factors include age, alcohol and tobacco use, poor nutrition, and conditions such as chronic oesophagitis for adenocarcinoma. Such pathology, particularly strictures and tumours cause gradual symptoms like progressive dysphagia (first for solids and then liquids), anorexia, regurgitation, chest or back pain and, finally, profound weight loss. The nutritional state often is not compromised until late because patients learn to modify their eating habits to cope with symptoms (like taking a soft diet); this poses problems for diagnosis in cases of more sinister pathology, and treatment is unlikely to have a positive effect on outcome.

Investigation is by endoscopy, barium studies, and computed tomography (CT) scans, which can identify most abnormalities, as well as help with staging. Treatment is decided by the extent of the disease; with surgery being the preferred option for local disease, the procedure also allows for lymph node dissection. Radiation helps with relief of symptoms like dysphagia. Subsequent studies have reported combination therapy to be beneficial owing to the high risk of distant metastases as well as local complications of the cancer.<sup>29</sup> Preoperative chemotherapy and radiation has been shown to decrease tumour size thus facilitating surgery and reducing the occurrence of distant metastases.<sup>30</sup>

Newer treatments include the use of Nd:YAG (neodymium-doped yttrium aluminum garnet) laser and photodynamic therapy, but these are only available in specialist centres and only a few large scale studies have demonstrated significant benefit over current treatment. Stenting remains a useful method of palliation in malignant disease, particularly where strictures have developed, either as a consequence of the underlying process or treatment (for example, radiotherapy). Various covered and uncovered metal stents are used, with excellent success rates: symptoms are relieved in 83–100% of patients.<sup>31</sup> Complications include migration (more with covered stents), bleeding, pain and more seriously, tumour overgrowth and subsequent blockage, particularly of uncovered stents. This is usually dealt with by laser therapy or re-stenting.

### STOMACH

The stomach undergoes major age related changes that have significant impact on disease processes that can occur. The following are the most important:

- Gastric atrophy
- Decreased gastric acid secretion
- Decreased pepsin
- Decreased mucus production and mucosal prostaglandin levels
- Reduced gastric emptying owing to slowing of transit time
- Reduced blood supply which may be exacerbated by generalised atherosclerotic disease in the older patient.

### Peptic ulcer disease

Peptic ulcer disease is frequently the result of impaired host protective responses to irritant stimuli like infections and drug use. The widespread use of NSAIDs in the elderly makes this an important contributory risk factor. The decreased mucus production and mucosal prostaglandin levels confer reduced mucosal protection.<sup>32</sup> Prostaglandins stimulate bicarbonate production, and NSAID mediated damage to gastric mucosa is through impaired mucus and bicarbonate secretion via their anti-prostaglandin effect. Slow transit times and reduced emptying result in prolonged exposure to these irritant drugs, with resultant erosive disease. A consequence of atrophy is reduced gastric acid secretion and pepsin production,<sup>33</sup> and this may be responsible for the reduced dilutional effect on irritant agents. The effect on drugs requiring acid breakdown may affect the bioavailability of such agents. Lastly, the ability of the gastric mucosal epithelium to repair itself after injury is reduced and this may explain why the older patient is more susceptible to recurrences of peptic ulcer disease.

NSAID use in the older patient is increasing, partly for analgesia in conditions like osteoarthritis and, more importantly, as prophylaxis for a thrombotic tendency in cardiovascular disease. Although this offers protection against cardiovascular mortality, it increases the tendency to gastric or duodenal ulcers, particularly if low dose aspirin is combined

with other anti-inflammatory drugs. Smoking in this age group doubles the risk.<sup>34</sup> There is a dose-dependent relationship and lower doses are associated with fewer side effects and less GI tract damage.<sup>35</sup> Although the possibility of complications is real, the evidence points to significant risk reduction in mortality from conditions such as strokes, myocardial infarctions, and Alzheimer's dementia. It seems obvious that independent patient risks need to be assessed and past history and comorbidities play an important role in decision making as to when treatment with NSAIDs can be safely instituted. Furthermore, the concurrent use of drugs that reduce gastric acid secretion or provide mucosal protection (for example, misoprostol) has been shown to reduce adverse effects in the elderly.<sup>36</sup>

### ***Helicobacter pylori* infection**

*Helicobacter pylori* infection is another leading cause of gastrointestinal injury and indeed the prevalence of this infection increases with age. Some estimates indicate that as many as 80% of the very elderly are affected.<sup>37</sup> The infection is common enough for a good number of physicians to limit screening for the condition in the elderly. The reluctance to perform endoscopic evaluation is not entirely without reason and studies have shown that the older patient is more at risk from the effects of sedation and needs smaller doses and closer monitoring during such procedures.<sup>38</sup> However, there are non-invasive tests (see below) and the decision to test will depend on individual patient circumstances.

The effect of *H. pylori* on the gastric mucosa in the elderly varies from ulceration to an inflammatory response with atrophic pan-gastritis and its negative association with reflux oesophagitis.<sup>26</sup> Even though *H. pylori* and NSAID use are independent risk factors for the development of ulcers, recent studies have shown that the two may have a synergistic effect on risk in geriatric patients.<sup>39-40</sup> A recent review highlighted the suggestion that eradication of *H. pylori* in a patient already receiving an NSAID, does not reduce the risk of NSAID-induced ulcers or bleeding. However, if about to start long term NSAID treatment, then treatment of *H. pylori* might reduce the overall risk of ulceration. This suggestion was based on two studies, which also showed that concomitant administration of a PPI could help in healing rates for ulcers, should they occur.<sup>41-42</sup>

However, not all ulcer disease is a consequence of *H. pylori*; some studies have described *H. pylori* negative ulcer disease.<sup>43</sup>

Besides gastroduodenal ulceration, both gastric adenocarcinoma and gastric lymphoma are associated with *H. pylori* infection, making this organism a carcinogen, particularly among Oriental Asians.<sup>44</sup> The classic presentation is one of burning epigastric pain usually occurring after meals and also awakening the patient at night. These attacks can last for weeks to months, depending on severity. The presence of symptoms like anorexia, dysphagia, upper GI bleeding, vomiting, weight loss, and unexplained anaemia suggest more sinister pathology and indicates the need for an urgent endoscopy.

Diagnosis is important and can be established by non-invasive means in the first instance, particularly in the absence of sinister symptoms. Serological testing for the presence of IgG antibodies is highly sensitive but cannot be used for follow-up because the antibodies remain high for at least a year.

The urea breath test also offers a relatively inexpensive means of testing and measures the carbon dioxide produced from the metabolism of radiolabelled [<sup>13</sup>C]urea by the bacterium. Sensitivity and specificity is high,<sup>45</sup> but both false positive and false negative results can occur; for this reason it is advised to stop all drugs like antibiotics and acid inhibiting drugs for at least a week before testing.

The rapid urease test at endoscopy offers the simplest method of testing for the presence of *H. pylori*. It is based on the ability of

an indicator system to detect the pH change induced by the urease enzyme derived from the organism (the CLO test is one such system that is cheap and reliable). In the elderly, results should be read with caution as there is a lower sensitivity, particularly in those above 60, than in younger adults.<sup>46</sup> In this situation, gastric biopsy offers an alternative, though the site must be considered carefully. Tissue sampling from the fundus or the body offers a better chance of a positive result than the antrum. Besides the effect of anti-secretory drugs, atrophic gastritis is common in this age group and can affect the outcome of such testing.

After testing, a decision must be made to treat and indeed, recent evidence suggests that the elderly benefit a great deal from eradication therapy. The decision to treat should be based on confirmation of *H. pylori* infection, and the cost savings of treatment balanced by the increased risk of unpleasant side effects while receiving antibiotic treatment, and the development of resistance if other bacteria are present.<sup>47</sup> Standard regimens with antibiotic and PPI combinations are used and confirmation of cure is obtained by the urea breath test, which is carried out 4–6 weeks after completion of treatment. The use of PPIs must be discontinued a week before testing to avoid interference with test results.

In the drive to reduce the prevalence of GI side effects of NSAIDs, cyclo-oxygenase inhibitors were briefly popular. However, drugs such as celecoxib and rofecoxib have been shown in recent trials to have an increased tendency to lead to cardiovascular complications like myocardial infarction and strokes, side effects which have prompted the withdrawal of rofecoxib from the market and the need for warning labels on packaging for celecoxib.<sup>48</sup> Thus the side effects of drugs are of added importance in the elderly, and their use merits careful evaluation of risks for each patient.

A mention must also be made of the way in which gastric pathology like atrophic gastritis can affect the bioavailability of nutrients and lead to deficiency states and malabsorption. Vitamin B12, folate, iron, and calcium are such nutrients whose digestion, metabolism, and intestinal uptake can be compromised as a result of inadequate acid and/or pepsin through poor solubility and receptor binding.<sup>49</sup> A more detailed description of malabsorption is given below.

### **SMALL INTESTINE**

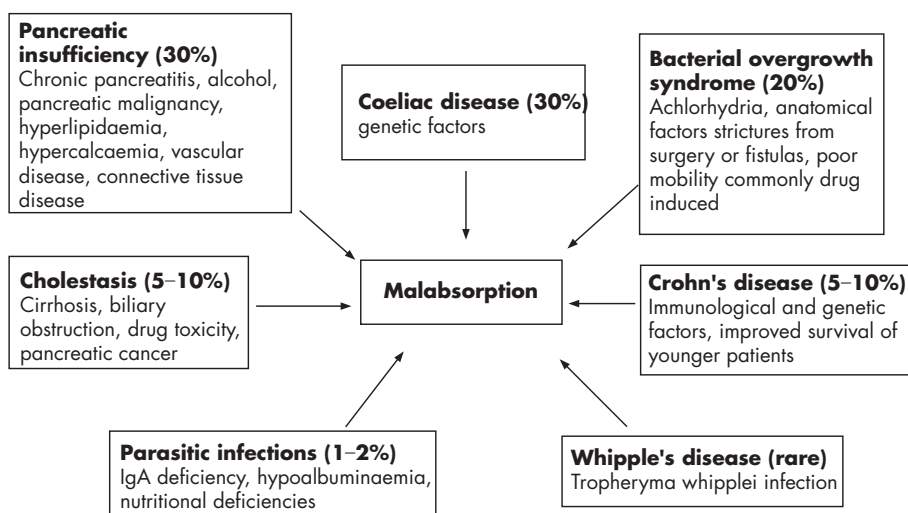
Physiological changes occur in the small bowel; but previous suggestions that these were cofactors in disease aetiology are now largely redundant. Indeed, the hormonal secretions and absorptive function of the small bowel are rarely limited in old age, except by disease. Both mucosal anatomy and absorptive capacity for most nutrients are well preserved<sup>50</sup>; however, a reduced adaptive reserve for these functions is also known.<sup>51</sup> Furthermore, there are minimal changes in motility and although changes in mucosal immunity do occur, these only achieve clinical significance in the presence of coexisting illness.

### **Malabsorption**

In other words, malabsorption is a result of disease of the GI system rather than ageing. This is one of a number of pathologies in the small bowel that are considerably important in geriatric patients and has a multifactorial aetiology (fig 3).<sup>52</sup>

The clinical manifestations of malabsorption are often subtle in the older person, leading to diagnostic delays. Abdominal symptoms like anorexia, nausea, diarrhoea, abdominal pain, bloating, and excessive flatus are sufficiently non-specific to occur in any one of the likely causes of malabsorption. Steatorrhoea is, however, the cardinal symptom of malabsorption and when this occurs, thorough investigation is merited to elicit a cause. Frequently, the manifestation is due to an





**Figure 3** Common causes of malabsorption in the elderly (adapted from the *Merck Manual of Geriatrics*).<sup>52</sup>

underlying deficiency, and features like anaemia, hypoalbuminaemia, osteoporosis; and neuromuscular symptoms like cramp and parasthaesiae are recognised effects of the lack of particular nutrients. Calcium absorption, in particular, is known to decrease with age and more readily explains the occurrence of bone disease in both men and women, thereby necessitating increased dietary requirements.

### Coeliac disease

Recently, coeliac disease has acquired importance in the older patient as an important cause of malabsorption and poor nutrition,<sup>53</sup> and numerous studies have raised the possibility that this condition is underdiagnosed in the elderly. Swinson and Levi showed that 25% of adult coeliac disease was diagnosed at 60 years or older and 2–10% diagnosed after the age of 70. Remarkably, in one study almost 50% of older patients had no GI symptoms at all,<sup>54</sup> although this has been disproved by a recent study.<sup>55</sup> Gasbarrini and colleagues demonstrated that 40% of elderly patients were diagnosed at >65 years and were more likely to present with abdominal and GI symptoms than younger adults.<sup>55</sup> Furthermore, the mean (SD) diagnostic delay in the elderly group was 17 (19) years (range 0–58).

There is a female preponderance of coeliac disease in younger adults, but in the elderly, men are the more likely sufferers. Other predisposing factors include inadequate diet, social deprivation, poor dentition, and cognitive impairment.<sup>56</sup> Diagnostic difficulty is experienced, primarily owing to co-existing pathologies; symptoms are non-specific and can include non-intestinal features. Diarrhoea is common but constipation is also recognised. Glossitis, aphthous ulcers, bone pain, and neurological features like ataxia can occur and are related to underlying nutritional deficiencies.<sup>57</sup> Numerous conditions are associated with coeliac disease and these include dermatitis herpetiformis—10% of these cases occur in people >60 years. Other known associations are diabetes mellitus, thyroid disease, and inflammatory bowel disease, through shared histocompatibility antigens. It has also been found that diabetic control is difficult and improves on a gluten-free diet.<sup>58</sup>

Diagnosis of coeliac disease is by serological screening tests and by demonstrating villous atrophy on duodenal biopsy, which is reversed on a gluten-free diet. Sorell and colleagues have demonstrated a screening test that detects IgA and IgG anti-tissue transglutaminase antibodies (anti-tTG), which are highly sensitive and specific for coeliac disease.<sup>59</sup> In some centres this has supplanted endomysial antibody serology as

the preferred test. Adherence to a gluten-free diet remains the cornerstone of treatment; in addition, replacement of vital nutrients, vitamins, and minerals is often required. There is an increased tendency to small bowel lymphoma in old age. This risk is reduced by prompt treatment through dietary manipulation, as described above.<sup>60</sup>

### Anaemia

A special mention must also be made of the tendency to anaemia which may be microcytic—owing to iron deficiency, or macrocytic—owing to vitamin B12 or folate deficiency, and is often the first manifestation of malabsorption. It can be as a result of reduced physiological function of the gastric mucosa that is known to occur in the elderly. Reduced production of intrinsic factor and gastric acid can interfere with the metabolism of vitamin B12 and iron. Microcytic anaemia in the absence of GI blood loss commonly indicates malabsorption of iron.

Food cobalamin malabsorption is the commonest cause of B12 deficiency in the elderly (60–70% of cases) while pernicious anaemia accounts for 15–20%.<sup>61</sup> Cobalamin malabsorption commonly results from distortion of local anatomy (previous gastric surgery or resection of small intestine), Crohn's disease, coeliac disease, Whipple's disease, chronic alcoholism, or even diphyllobothrium infections.<sup>62</sup>

Chronic carriage of *H. pylori*, drugs like metformin, even H2 blockers or PPIs may also be contributory<sup>63</sup> and small intestinal bacterial overgrowth is an important aetiological factor, particularly in the elderly infirm. This overgrowth can result from hypochlorhydria and decreased mobility and occurs in 15–50% of the older population.<sup>64</sup>

Pernicious anaemia is another important cause of B12 deficiency and is an autoimmune condition where there is a lack of intrinsic factor owing to destruction of the gastric mucosa. Antibodies are commonly detected, these include anti-intrinsic factor and anti-gastric parietal cell antibodies which are sensitive, but not specific for this condition.<sup>65</sup> Gastric mucosal biopsies are performed regularly and demonstrate atrophy and the absence of *H. pylori*. It should be borne in mind that an atrophic stomach is easily irritated causing reflux of acid and gastritis/esophagitis. Ulcers form and the resultant upper GI bleeding can lead to iron deficiency anaemia.

In people >65 years, GI blood loss remains the commonest cause of iron deficiency; it is rare that iron deficiency will result from poor nutritional intake alone. Prolonged achlorhydria may

also contribute to iron deficiency through a reduced conversion of ferric to ferrous iron, a process that requires an acidic state.<sup>66</sup>

If a deficiency of B12 is confirmed, further investigations include thyroid function tests and other tests for malabsorption. These include blood tests like a peripheral smear, iron and ferritin levels, calcium profile (which includes a serum albumin), and serum or red cell folate. Tests for steatorrhoea (fecal fat, C14 breath test), mucosal integrity (D-xylose test, which can help differentiate pancreatic exocrine insufficiency from intestinal mucosal disease), and tests of pancreatic exocrine function (fecal elastase test or pancreolauryl test)<sup>67</sup> are also necessary.

An important consideration is whether elderly people should be screened for the presence of B12 deficiency in the face of the increased occurrence of malabsorption. The current recommendations are that people >65 years, malnourished people, those in nursing and residential homes, and older people with neuropsychiatric problems would benefit from annual screening.<sup>68</sup> Treatment of malabsorption involves treating the underlying causes and replacing deficient nutrients like iron, calcium, and vitamins.

### Diarrhoea

Diarrhoea can be an important symptom of small bowel disease and may be acute or chronic. It is characterised by an increased liquidity of stool with an associated increase in frequency and volume.

The elderly are more susceptible to diarrhoea owing to factors like hypochlorhydria or achlorhydria, exposure to enteropathogens, luminal stasis, decreased mucosal immunity, and the use of drugs such as antibiotics.<sup>69</sup> Acute diarrhoea is usually infectious and is more likely to occur with increasing severity in elderly infirm patients, with consequent increased mortality (16–35%),<sup>70</sup> though a recent study showed no greater mortality as a consequence of *Clostridium difficile* disease.<sup>71</sup> Bloody diarrhoea can occur in conditions such as bowel ischaemia and inflammatory bowel disease. Chronic diarrhoea may be secretory (which often results from the secretion of water and electrolytes into the bowel as a result of hormonal stimulation) or osmotic (secondary to food solutes or drugs like laxatives and antacids). Indeed, drug induced causes of diarrhoea are important in the elderly and the mechanisms of causation are diverse. Disruption of GI tract defences (PPIs alter gastric acid secretion, anticholinergics affect intestinal motility or even the depletion of intestinal flora by antibiotics) is one way drugs can cause diarrhoea. Others include damage to the mucosal surface (microscopic colitis) and impaired fluid absorption and secretion owing to drug-induced effects on the absorbing surface, transport mechanisms, and gut motility.<sup>72</sup> The elderly are more susceptible to dehydration and systemic toxicity as a result. It is therefore more important to treat diarrhoea more aggressively by fluid replacement and early diagnosis of potential causes.

A special mention must be made of nosocomial diarrhoea. Age affects the intestinal microflora, with a decrease in anaerobes and bifidobacteria and an increase in enterobacteria. These changes coupled with a reduced gut immune response make many elderly people susceptible to infectious diarrhoea.<sup>73</sup> The liberal use of antibiotics in hospitals and in the community has resulted in an increased incidence of *antibiotic-associated diarrhoea* and *Clostridium difficile associated diarrhoea*, with its consequent morbidity and mortality, not to mention increased costs.

In addition to standard treatment with metronidazole and vancomycin, newer approaches to treatment of this condition include the use of probiotics, which have been shown in various studies and recent meta-analyses to have beneficial results.<sup>74</sup> Both *Lactobacilli* (odds ratio 0.34, confidence interval 0.19 to 0.61) and the yeast *Saccharomyces boulardii* (odds ratio 0.39,

confidence interval 0.25 to 0.62) were found to be more beneficial than placebo in the prevention of diarrhoea. Their acceptance into clinical practice together with a modification of antibiotic policies and infection control procedures can have a significant impact on the prevalence of this condition.

### Mesenteric ischaemia

Mesenteric ischaemia is an important cause of abdominal pain in the older patient and can present as acute or chronic disease. It usually results from the occlusion of branches of the coeliac axis by either clot or thrombus. Splanchnic blood flow is known to decline with age, both in absolute terms and as a fraction of cardiac output. This makes the mesenteric bed more susceptible to hypoxia and hypovolaemic injury.<sup>75</sup> A recent review by Kozuch *et al* described the variants of intestinal ischaemia that are commonly seen<sup>76</sup>; of these, superior mesenteric artery embolus is the commonest cause (50% of cases) followed by non-occlusive mesenteric ischaemia (NOMI) in 25%, and superior mesenteric artery thrombus in 10% of cases. For all these conditions, old age is a risk factor along with the presence of cardiovascular disease—in particular, atherosclerosis, ischaemic heart disease, and atrial fibrillation.

NOMI remains the predominant presentation of bowel ischaemia in the elderly patient and is seen more often after cardiopulmonary bypass operations.<sup>77</sup> It also tends to occur as a result of sustained vasoconstriction as in hypovolaemia, acute myocardial infarction with shock, congestive heart failure, and sepsis. Abdominal pain is the hallmark of presentation, though in the elderly, this is seen less often and symptoms of acute confusion (29%) and tachypnoea (35%) predominate. Other features include nausea, vomiting, haematemesis, fever, abdominal distension with guarding, back pain, and shock.<sup>78</sup> In the chronic setting, post-prandial abdominal pain and weight loss are seen and an acute presentation may be superimposed.

Diagnosis is mainly by radiological tests. Angiography is the best for NOMI and allows the use of therapeutic options—namely, intra-arterial vasodilators. Other techniques include computed tomography (CT) or magnetic resonance angiogram, and an abdominal plain x ray examination remains useful as a complement to CT imaging.<sup>79</sup>

Treatment involves general measures of fluid replacement, oxygen, and antibiotics that include metronidazole in the regimen. Specific measures such as thrombolysis are useful, though caution is advisable in the elderly. NOMI responds to the use of papaverine both pre- and postoperatively.<sup>80</sup> It must be emphasised that in treatment of intestinal ischaemia, dealing with the underlying disease or contributory pathology (for example, atrial fibrillation) is also important.

### LARGE INTESTINE

Ageing does not have a major effect on the large bowel. In particular, there are no major changes in colonic or rectosigmoid motility or indeed even in the capacity of water transport across the bowel wall.

### Constipation

The increased frequency of certain conditions like constipation in this age group lends weight to the argument that there are subtle changes in transit time along with lifestyle factors that have an important role in pathogenesis. Indeed, inactivity, poor hydration, inappropriate diet, depression, and drug treatment are important factors in the development of constipation.<sup>81</sup>

The spectrum of disease includes both functional constipation (difficult, infrequent or incomplete defecation) and rectal outlet delay (disorders associated with difficulty in defecation, necessitating straining and a feeling of incomplete evacuation). Constipation has a significant impact on the level of physical

function and quality of life in people >65 years.<sup>82</sup> In one study in America, prevalence rates were 24.4% for functional constipation and 20.5% for rectal outlet delay among 1375 older responders to a study questionnaire.<sup>83</sup> Symptoms of constipation, though different descriptions were given by respondents, were related to advancing age. Additionally, the use of drugs, including non-steroidal agents, was a significant risk factor in its development.<sup>82</sup> A particular risk factor in elderly women was pelvic floor dysfunction as a result of the effects of childbirth and pelvic surgery.<sup>84</sup> In reality, bowel frequency is largely unchanged in comparison with younger people, but older people confuse hard stools with constipation and a larger volume distension of the rectum is required to initiate defecation. The result is a tendency to retention and fecal impaction, frequently requiring the use of enemas or at times digital evacuation.

### Irritable bowel syndrome

Constipation can also occur as the predominant symptom of irritable bowel syndrome (IBS). Factors playing a part in the development of this problem in elderly patients are abnormal motility, increased sensation, and psychosocial disturbances. More recently, neuroimmune dysfunction is being investigated. It is suggested that the postinflammatory effect of gastroenteritis on neuromuscular function of the gut is responsible for postinfectious IBS, though a recent study disputed this.<sup>85</sup>

A significant number of older people report symptoms of IBS (as defined by the Rome II criteria); this varies from 10% to 20% in some studies.<sup>86</sup> Besides abdominal pain relieved by defecation, there is also a change in the frequency and form of the stools at the time of onset. Patients may also present with danger symptoms (anaemia, fever, weight loss, bleeding per rectum) and in this event, further investigation is mandatory, and should include a colonoscopy.

Treatment revolves around a symptomatic approach and involves lifestyle modification and use of pharmacological treatments. Fibre supplements, osmotic laxatives or stimulant laxatives are useful in constipation. For diarrhoea, loperamide or anti-spasmodic drugs are useful. Given that psychological factors have a role in pathogenesis, a trial of antidepressants is sometimes useful.<sup>87</sup> More recently, the use of 5HT<sub>3</sub> and 5HT<sub>4</sub> serotonin-receptor antagonists has been found to help by regulating motor and secretory function and also the sensations of pain and bloating.<sup>88</sup>

### Diverticular disease

Diverticular disease is also prevalent in elderly patients. It encompasses the entire spectrum of disease from asymptomatic diverticulae to the presence of inflammation or diverticulitis, particularly in the colon. It results from asymmetric contraction of the bowel wall, leading to segmentation and development of pulsion outpouchings in areas of weakness.<sup>89</sup>

Around a third of people with the condition are >60 years and two thirds are >80; the disease affects more women than men and contributes significantly to healthcare costs.<sup>90</sup> Although predominantly a disease of the West, where it is left-sided, it is also seen in Asia, where the condition is right-sided and tends to affect middle aged patients.<sup>91</sup>

Diverticular disease is related to a reduced fibre diet, and iatrogenic factors may also contribute to flare-ups in disease activity. NSAIDs can exacerbate colonic diverticulitis; a greater incidence of perforation has been noted in this setting, necessitating surgical treatment.<sup>92</sup> Furthermore, the disease is possibly related to the use of opiates in the older patient, and there is also a greater risk of developing *Clostridium difficile* associated pseudomembranous colitis after antibiotic use.<sup>93</sup>

Clinical features in the older patient are no different from those described in the literature: the presentation can vary from

mild episodes of inflammation with pain, fever, and lower GI bleeding to more severe features of abscess formation and perforation. There can, however, be a paucity of signs in the elderly.<sup>89</sup> A debate still rages about a relationship with IBS, though this is far from conclusive. The presence of ischaemia in the ageing bowel leads to narrowing and delayed transit, thereby contributing to pain and constipation, signs commonly attributed to IBS.<sup>94</sup> There is conflicting evidence on whether irritable bowel disease represents a prodrome in the development of diverticular disease; however, the relatively short history before presentation and the absence of prior symptoms make any relationship possibly coincidental.<sup>95</sup>

Diagnosis rests on the use of colonoscopy and imaging and it is important to rule out the presence of colonic neoplasms, which share many presenting features. A CT scan with contrast is the preferred test in the elderly as an alternative to a barium enema, as it allows simultaneous percutaneous drainage of a diverticular abscess. Bowel rest and antibiotics remain the mainstay of treatment of diverticulitis; if no improvement occurs in 48 hours, a CT scan is mandatory and a surgical opinion should be sought. Furthermore, there is little doubt that there is an increased risk of complications as a result of surgery in the older patient.<sup>96</sup> Lifestyle modification such as increasing exercise, reducing fat intake, and increasing dietary fibre can prevent attacks of diverticulitis.<sup>97</sup> Despite recent advances in the treatment of various abdominal symptoms like pain, bloating, and constipation, the morbidity and cost implications of diverticular disease in the elderly continue to be important.

### Colorectal cancer

Colorectal cancer (CRC) is another large bowel condition that is predominantly a disease of the elderly; 90% of colon cancers occur in people aged >50 years, and 20–40% are seen in men and women aged 80 years or older.<sup>98</sup>

The causes and risk factors are diverse and include dietary, geographical, and genetic factors. Indeed, there is two- to threefold increase in the risk of cancer in first degree relatives of affected cases compared with those without a family history. Most cancers arise from pre-existing adenomatous polyps and given the familial tendency, screening is merited.<sup>99</sup>

The current recommendations for screening are tailored to early detection; colonoscopy should start at 50 years in those with average risk but at 40 years for those with a family history of CRC.<sup>100</sup> A combination of fecal occult blood testing, flexible sigmoidoscopy and in certain cases, double contrast barium enema is associated with good detection rates and correlates with improved survival outcomes by 30–40%.<sup>101</sup> A great debate has ranged as to the optimal method of screening for large bowel cancer. The lack of sensitivity and indeed specificity of fecal occult blood testing precludes its acceptance by many clinicians. However, having been subject to the rigours of a randomised controlled trial, it has been shown to reduce mortality from CRC by 30% through early identification of patients requiring further investigation. Furthermore, occult blood testing using modern immunochemical techniques has shown improved sensitivity and specificity.<sup>102</sup> There is no doubt that it offers a simple painless way of self testing (the patient collects two consecutive stool specimens) and in conjunction with the other screening methods, aids in the diagnosis of large bowel cancer.

Survival figures are poor in the elderly, in addition to disease mortality; the risks of treatment are also high and there is a well known reluctance to institute treatment options on this basis. Older age is an independent predictor of short and long term mortality after surgery for both rectal and colon cancer, and surgical resection for bowel cancer is not a commonly exercised option.<sup>103</sup> Part of the problem in the elderly is that a



significant number of cases of CRC present acutely (20%); consequently, there is a tendency for emergency surgery in this age group with all its inherent complications, leading to an increased postoperative mortality.<sup>104</sup> However, the previously held belief that older patients do worse after bowel surgery has been disputed by the findings of a recent study, that demonstrated no reduction in survival as a consequence of the cancer.<sup>105</sup>

The advent of advanced surgical techniques has been of particular benefit to the older patient with bowel cancer. In one study, patients treated by this method recovered faster and had reduced morbidity.<sup>106</sup> Indeed, laparoscopic colonic resection was associated with decreased postoperative pain, early return to normal bowel function, lower cardiopulmonary risk, and shorter hospital stay. There is some concern, however, about a limited surgical field, port-site metastasis, and long term outcomes of minimally invasive operations. The need for open laparotomy conversion, currently 11–22%, is also a point for discussion; though this is often the result of delays in diagnosis owing to unusual presentations.<sup>107</sup> Despite these concerns, the use of laparoscopy remains a safe and effective surgical technique in elderly patients.

The use of chemotherapy as a means of treatment is also advocated in this age group; studies have confirmed its effectiveness when used as an adjunct to surgery. Fata *et al* remarkably demonstrated an improved survival in the over 65 age group of patients (70%) compared with younger counterparts (56%) ( $p = 0.085$ ).<sup>108</sup> Standard regimens of 5-fluorouracil in combination with levamisole or folinic acid are useful in both locally advanced and metastatic disease. Radiotherapy is also a useful treatment option; when used in conjunction with chemotherapy for stage B and stage C rectal tumours. It has been shown to reduce local recurrence and improve survival.<sup>109</sup> It is hoped these studies will remove the major prejudices against the aggressive treatment of CRC in the elderly.

Difficulty remains when bowel cancers present insidiously: delays mean more complicated scenarios and metastatic disease at first presentation. A mention must be made of colorectal stents and their use for bowel decompression in these situations. Stenting may be temporary in acute malignant obstruction (where it allows bowel preparation and elective surgery), or even used as a palliative step for unresectable tumours. Studies have shown a clinical success rate of 84–100% and a complication rate of 14–42%.<sup>110</sup> Most complications were minor (migration of the stent), but perforation and sepsis also occurred.

A particular alarm symptom in the elderly, is anaemia of chronic disease, which should prompt a search for potential causes. An appropriate plan of investigation should include:

- Confirmation and typing of anaemia
- Fecal occult blood testing
- Gastrointestinal tract visualisation (both upper and lower bowel) by endoscopy
- Barium enema (with air contrast), especially in the presence of bowel symptoms. CT colonography is now increasingly being used instead, particularly in the elderly, when pain, bowel stenosis or strictures are limiting factors and difficulties are expected with colonoscopy.<sup>111</sup> This is a helical CT examination in which the air-distended colon is evaluated by three dimensional imaging for the presence of polyps and cancer. It uses a dry bowel preparation with oral barium as contrast, permitting better visualisation of the bowel wall. Although it has a high accuracy, recent studies have shown a reduced sensitivity in detection of polyps 10 mm in size, in comparison with colonoscopy (59% *v* 98%,  $p < 0.0001$ ).<sup>112</sup> It can be a useful adjunct to colonoscopy; the

segmental unblinding technique uses endoscopic visualisation of a bowel segment to evaluate false positive lesions detected by scanning.

- Specialist centres may even be able to offer radioisotope scans to confirm the presence of occult GI blood loss.

Although the older patient with bowel cancer frequently has comorbidities, it is now evident that treatment of cancer in this group of patients has results comparable with those of the average adult population and should be actively pursued in the right clinical setting.

## CONCLUSION

Gastroenterology in the geriatric patient remains an important aspect of clinical medicine and requires high prioritisation for development of treatment protocols of common GI conditions. The approach should include consideration of physiological effects of ageing on the gut to help tackle the underlying pathological processes involved; it is rare that the effects of ageing alone are sufficient to explain the manifestations of disease. The older patient requires specific treatments often involving primary care physicians, geriatricians, and gastroenterologists. Age should not be a limiting factor when considering investigations, though these are very often hampered by a lack of physical fitness for such procedures. There is now convincing evidence of improvement in clinical outcomes in the elderly after treatment, from conditions as common as heartburn and GORD to the more severe carcinoma of the bowel. The strain on public health services by older patients requires greater emphasis to be placed on early identification and treatment of common conditions, so as to prevent long term morbidity and indeed the mortality that so often results.

No conflict of interest declared.

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